

I. AMENDMENT

In the specification

At page 1, after the title, please insert the following sentence.

-- This application is a 35 U.S.C. §371 filing of International Patent Application No. PCT/EP97/05441, filed October 2, 1997. This application claims priority benefit of German Patent Application No. DE 19640817.2, filed October 2, 1996.

In the Claims:

Please cancel claims 1-41, without prejudice or disclaimer. Please add new claims 42-82, shown below.

42. A method for producing a complete gp190/MSP1 protein of a *Plasmodium*, comprising expressing a nucleotide sequence encoding the complete gp190/MSP1 protein in an expression vector, wherein the AT content of the expressed nucleotide sequence encoding the complete gp190/MSP1 protein is less than the AT content of a naturally occurring nucleotide sequence encoding a gp190/MSP1 protein.

43. The method of claim 42, wherein the *Plasmodium* is a strain of *Plasmodium falciparum*.

44. The method of claim 43, wherein the strain of *Plasmodium falciparum* is *P. falciparum* strain FCB-1.

45. The method of claim 42, wherein the AT content is reduced from about 74% to 55%.

46. The method of claim 42, wherein the nucleotide sequence encoding the complete gp190/MSP1 is denoted gp190s in Figure 3C.

47. The method of claim 42, wherein the nucleotide sequence encoding a gp190/MSP1 protein further comprises a nucleotide sequence encoding an attachment signal.

See Fig

Docket No. 402162000200

48. The method of claim 42, wherein the nucleotide sequence encoding a gp190/MSP1 protein further comprises a nucleotide sequence encoding a signal peptide.

49. The method of claim 42, wherein nucleotide sequence encodes a gp190/MSP1 having the amino acid sequence selected from the group consisting of amino acids 1-1639, 1-1621, and 20-1621, depicted in Figure 3C.

50. The method of claim 1, wherein the nucleotide sequence encoding the complete gp190/MSP1 protein is produced according to a method comprising:

- (a) designing a nucleotide sequence encoding a gp190/MSP1 from a *Plasmodium* to contain codon frequencies common in the human genome, while maintaining the encoded gp190/MSP1 protein;
- (b) dividing the sequence of step (a) into individual overlapping regions;
- (c) synthesizing desoxynucleotides each extending the whole length of each individual region of step (b);
- (d) cloning the individual region coding sequences; and
- (e) fusing the regions to produce a sequence encoding gp190/MSP1.

51. The method of claim 50, wherein the nucleotide sequence being designed encodes a gp190/MSP1 protein from *Plasmodium falciparum* FCB-1, and the overlapping regions of step (b) encode p83, p31, p36, p30, and p19, and wherein the method further comprises a step (c') which is performed after step (c) and comprises synthesizing coding regions encoding gp19, gp30, p36 and p31 by polymerase chain reaction and synthesizing a coding region encoding p83 by fusion of two sequences comprising approximately 1200 bp.

52. The method of claim 50, wherein the desoxyoligonucleotides synthesized in step (c) are on average 120 nucleotides long, and wherein the overlap between individual regions is about 20 bases.

53. The method of claim 42, wherein the expression vector is selected from the group consisting of dPS56RBSII, pBi-5, and ppTMCS.

54. The method of claim 42, wherein the nucleotide sequence is expressed in an *Escherichia coli* (*E. coli*) strain.

55. The method of claim 54, wherein the *E. coli* strain is DH5alphaZ1.

56. The method of claim 42, wherein the nucleotide sequence is expressed in an expression system selected from the group consisting of HeLa cells and CHO cells.

57. The method of claim 42, wherein the nucleotide sequence is expressed in an expression system selected from the group consisting of Toxoplasma gondii and Leishmania.

58. A nucleotide sequence encoding a complete gp190/MSP1 protein of a *Plasmodium*, wherein the AT content of the nucleotide sequence encoding the complete gp190/MSP1 protein is less than the AT content of a naturally occurring nucleotide sequence encoding a gp190/MSP1 protein.

59. The nucleotide sequence of claim 58, further comprising a nucleotide sequence encoding an attachment signal.

60. The nucleotide sequence of claim 58, further comprising nucleotide sequences encoding a signal peptide.

61. The nucleotide sequence of claim 58, wherein the sequence further comprises a sequence encoding an N-terminal extension of about 11 amino acids, of which six are histidine.

62. The nucleotide sequence of claim 58, wherein the sequence lacks sequences that function as splice donor and splice acceptor signals.

- 63. The nucleotide sequence of claim 58, wherein the sequence lacks a region comprising GC-rich sequences.
- 64. The nucleotide sequence of claim 58, wherein the sequence lacks recognition sequences for restriction enzymes which recognize sequences of six or more base pairs.
- 65. The nucleotide sequence of claim 58, wherein the nucleotide sequence comprises one or more cleavage sites for restriction endonucleases, and wherein each of said cleavage sites occurs no more than once in said nucleotide sequence.
- 66. The nucleotide sequence of claim 58, further comprising cleavage sites for endonucleases at the 5' and 3' ends of the nucleotide sequence, said endonuclease cleavage sites being absent from the remainder of the nucleotide sequence and from an expression or cloning vector containing said nucleotide sequence.
- 67. The nucleotide sequence of claim 58, wherein the nucleotide sequence encoding the complete gp190/MSP1 consists of a sequence denoted gp190s in Figure 3C.
- 68. The nucleotide sequence of claim 58, wherein the AT content is reduced from about 74% to about 55%, compared to the AT content of the naturally occurring nucleotide sequence.
- 69. The nucleotide sequence of claim 58, wherein nucleotide sequence encodes a gp190/MSP1 having the amino acid sequence selected from the group consisting of amino acids 1-1639, 1-1621, and 20-1621 of the sequence denoted gp190s in Figure 3C.
- 70. A vector comprising the nucleotide sequence of claim 58.
- 71. The vector of claim 70, wherein the vector is an expression vector.
- 72. The vector of claim 71, wherein the expression vector is selected from the group consisting of dPS56RBSII, pBi-5, and ppTMCS.
- 73. A host organism comprising the nucleotide sequence of claim 58.

74. The host organism of claim 73, wherein the host organism is an *Escherichi coli* (*E.coli*) strain.

75. The host organism of claim 74, wherein the *E. coli* strain is DH5alphaZ1.

76. The host organism of claim 73, wherein the host organism is a cell selected from the group consisting of a HeLa cell and a CHO cell.

77. The host organism of claim 76, wherein the cell constitutively synthesizes a tetracycline transactivator.

78. The host organism of claim 73, which is selected from the group consisting of *Toxoplasma gondii*, *Leishmania*, baculovirus, adenovirus, and yeast.

79. A method of delaying development of malaria parasite *Plasmodium* parasitemia in an animal, comprising administering gp190/MSP1 to the animal.

80. A composition for use as a vaccine, said composition comprising a nucleotide sequence according to claim 58.

81. A composition comprising a host organism according to claim 73.

82. A method for stabilizing a gene sequence, comprising reducing the AT content of the sequence, compared to the AT content of the naturally occurring gene sequence.

II. REMARKS

The PCT application contained claims 1-41. By this Preliminary Amendment, Applicants have cancelled original claims 1-41, without prejudice or disclaimer, and have added